

WHAT IS CLAIMED IS:

1. A purified and isolated polypeptide having part or all of the primary structural conformation and one or more of the biological properties of naturally-occurring pluripotent granulocyte colony-stimulating factor and characterized by being the product of procaryotic or eucaryotic expression of an exogenous DNA sequence.
2. A polypeptide according to claim 1 further characterized by being free of association with any mammalian protein.
3. A polypeptide according to claim 1 wherein the exogenous DNA sequence is a cDNA sequence.
4. A polypeptide according to claim 1 wherein the exogenous DNA sequence is a manufactured DNA sequence.
5. A polypeptide according to claim 1 wherein the exogenous DNA sequence is a genomic DNA sequence.
6. A polypeptide according to claim 1 wherein the exogenous DNA sequence is carried on an autonomously replicating DNA plasmid or viral vector.
7. A polypeptide according to claim 1 possessing part or all of the primary structural conformation of human pluripotent granulocyte colony-stimulating factor as set forth in Table VII or any naturally occurring allelic variant thereof.

8. A polypeptide according to claim 1 which has the immunological properties of naturally-occurring pluripotent granulocyte colony-stimulating factor.

5 9. A polypeptide according to claim 1 which has the in vitro biological activity of naturally-occurring pluripotent granulocyte colony-stimulating factor.

10 10. A polypeptide according to claim 1 further characterized by being covalently associated with a detectable label substance.

11. A polypeptide according to claim 10  
15 wherein said detectable label is a radiolabel.

12. A DNA sequence for use in securing expression in a procaryotic or eucaryotic host cell of a polypeptide product having at least a part of the  
20 primary structural conformation and one or more of the biological properties of naturally-occurring pluripotent granulocyte colony-stimulating factor, said DNA sequence selected from among:

(a) the DNA sequence set out in Tables VII  
25 and VII or their complimentary strands;

(b) DNA sequences which hybridize to the DNA sequences defined in (a) or fragments thereof; and

(c) DNA sequences which, but for the degeneracy of the genetic code, would hybridize to the  
30 DNA sequences defined in (a) and (b).

13. A procaryotic or eucaryotic host cell transformed or transfected with a DNA sequence according to claim 12 in a manner allowing the host cell to  
35 express said polypeptide product.

14. A polypeptide product of the expression of a DNA sequence of claim 12 in a procaryotic or eucaryotic host.

5 15. A purified and isolated DNA sequence coding for procaryotic or eucaryotic host expression of a polypeptide having part or all of the primary structural conformation and one or more of the biological properties of pluripotent granulocyte colony-stimulating  
10 factor.

16. A cDNA sequence according to claim 15.

15 16. 17. A genomic DNA sequence according to claim

18. A manufactured DNA sequence according to claim 15.

20 19. A manufactured DNA sequence according to claim 18 and including one or more codons preferred for expression in E. coli cells.

25 20. A manufactured DNA sequence according to claim 18, and coding for expression of human species pluripotent granulocyte colony-stimulating factor.

30 21. A manufactured DNA sequence according to claim 20 and including one or more codons preferred for expression in yeast cells.

35 22. A human species pluripotent granulocyte colony-stimulating factor-coding DNA sequence according to claims 16, 17 or 18.

23. A DNA sequence according to claim 15 covalently associated with a detectable label substance.

24. A DNA sequence according to claim 23  
5 wherein the detectable label is a radiolabel.

25. A single-stranded DNA sequence according to claim 23.

10 26. A DNA sequence coding for a polypeptide fragment or polypeptide analog of naturally-occurring pluripotent granulocyte colony-stimulating factor.

15 27. A DNA sequence coding for [Ala<sup>1</sup>] hpG-CSF.

28. A biologically functional plasmid or viral DNA vector including a DNA sequence according to one of claims 12, 15 or 26.

20 29. A procaryotic or eucaryotic host cell stably transformed or transfected with a DNA vector according to claim 28.

25 30. A polypeptide product of the expression in a procaryotic or eucaryotic host cell of a DNA sequence according to claims 15 or 26.

30 31. A synthetic polypeptide having part or all of the amino acid sequence as set forth in Table VII and having one or more of the in vitro biological activities of naturally-occurring pluripotent granulocyte colony-stimulating factor.

35 32. A synthetic polypeptide having part or all of the secondary conformation of part or all of the amino acid sequence set forth in Table VII and having a

biological property of naturally-occurring human pluripotent granulocyte colony-stimulating factor.

33. A process for the production of a polypeptide having part or all of the primary structural conformation and one or more of the biological properties of naturally occurring pluripotent granulocyte colony-stimulating factor, said process comprising:  
growing, under suitable nutrient conditions,  
procaryotic or eucaryotic host cells transformed or transfected with a DNA vector according to claim 28, and isolating desired polypeptide products of the expression of DNA sequences in said vector.

34. Purified and isolated human pluripotent granulocyte colony-stimulating factor free of association with any human protein in glycosylated or non-glycosylated form.

35. A pharmaceutical composition comprising an effective amount of a polypeptide according to claims 1 or 34 and a pharmaceutically acceptable diluent, adjuvant or carrier.

36. A method for providing hematopoietic therapy to a mammal comprising administering an effective amount of a polypeptide according to claims 1 or 34.

37. A method for arresting proliferation of leukemic cells comprising administering an effective amount of a polypeptide according to claims 1 or 34.

38. A DNA sequence coding for  
[Ser<sup>17</sup>]hpG-CSF.

39. A polypeptide product of the expression in a procaryotic or eucaryotic host cell of a DNA sequence according to claim 38.

5           40. A biologically functional plasmid or viral DNA vector including a DNA sequence according to claim 38.

10           41. A procaryotic or eucaryotic host cell stably transformed or transfected with a DNA vector according to claim 40.

15           42. A DNA sequence coding for an analog of hpG-CSF selected from the group consisting of:  
[Ala<sup>1</sup>]hpG-CSF;  
[Ser<sup>36</sup>]hpG-CSF;  
[Ser<sup>42</sup>]hpG-CSF;  
[Ser<sup>64</sup>]hpG-CSF;  
[Ser<sup>74</sup>]hpG-CSF;  
20           [Met<sup>-1</sup>, Ser<sup>17</sup>]hpG-CSF;  
[Met<sup>-1</sup>, Ser<sup>36</sup>]hpG-CSF;  
[Met<sup>-1</sup>, Ser<sup>42</sup>]hpG-CSF;  
[Met<sup>-1</sup>, Ser<sup>64</sup>]hpG-CSF; and  
[Met<sup>-1</sup>, Ser<sup>74</sup>]hpG-CSF.

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43. A polypeptide product of the expression in a procaryotic or eucaryotic host cell of a DNA sequence according to claim 42.

30           44. A preparation of hpG-CSF which is greater than 95% pure and which comprises less than 0.5 ng of pyrogen per 0.5 mg of hpG-CSF.

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